The Effectiveness of Virtual Reality Interventions for Improvement of Neurocognitive Performance Post-traumatic Brain Injury: A Systematic Review.

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Declaration of Interest

The authors report no conflicts of interest.

Abstract

Objective: The aim of this study was to evaluate current evidence for the effectiveness of virtual reality (VR) interventions in improving neurocognitive performance in individuals who have sustained a traumatic brain injury (TBI).

Methods: A systematic literature search was performed across multiple databases (PubMed, EMBASE, Web of Science) for articles of relevance. Studies were evaluated according to study design, patient cohort, VR intervention, neurocognitive parameters assessed, and outcome. VR interventions were evaluated qualitatively, with respect to methodology and extent of immersion, and quantitatively with respect to intervention duration.

Outcomes: Our search yielded 324 articles, of which only 13 studies including 132 patients with TBI met inclusion criteria. A wide range of VR interventions and cognitive outcome measures were reported. Cognitive measures included learning and memory, attention, executive function, community skills, problem solving, route learning, and driving attitude. Several studies (n=10) reported statistically significant improvements in outcome, and two studies demonstrated successful translation into real-life performance.

Conclusions: VR interventions hold significant potential for improving neuro-cognitive performance in patients with TBI. Whilst there is some evidence for translation into activities of daily living, further studies are required to confirm the validity of cognitive measures and reliable translation into real-life performance.

Keywords: systematic review; virtual reality; traumatic brain injury; neurocognitive; rehabilitation

Abbreviations: TBI- traumatic brain injury; IADL- independent activities of daily living; VR- virtual reality

Introduction

Traumatic brain injury (TBI) is one of the leading causes of mortality and morbidity worldwide[1], contributing to approximately 30% of all injury-related deaths [2] in the United States. TBI can be divided into mild, moderate, and severe, depending on GCS at presentation, duration of PTA, and neurological deficits[3]. It is best understood as a pathophysiological entity involving an acute injurious trigger for a chronic process. This manifests, especially in moderate-severe TBI, as a multitude of deficits in sensorimotor, behavioural, and cognitive functions, such as attention, memory, executive function, and problem-solving skills [4,5]. This culminates in a considerable impact on everyday functioning, and necessitates a multidisciplinary approach to an individualised rehabilitation programme. Current approaches are hindered by factors such as inadequate access to care centres and limited clinical resources [6]. Furthermore, increasing survival rates due to advancing healthcare in this cohort corroborate the requirement for an adequate solution to this problem [7].

The advent of virtual reality (VR) technology and its incorporation into rehabilitation approaches may provide an answer. Ellis (1994) [8] defines VR as 'interactive, virtual image displays enhanced by special processing and by non-visual display modalities… to convince users that they are immersed in a synthetic space.' Since the time of this traditional definition of VR, rapid progress in technology means that it is increasingly possible to 'convince users that they are immersed' through various modalities such as head mounted displays, three dimensional (3D) displays, joysticks, gloves, and haptic feedback from robotic arms. Currently there is increasing evidence for the use of VR in cognitive rehabilitation in schizophrenia [9], depression [10], neurodegenerative disorders [11], and dementia [12]. Essentially, VR technology is proving to be a discernible tool in the assessment, diagnosis, and treatment of chronic neurological and psychiatric disorders. It is well suited to this purpose as it provides: (i) a safe environment to practise activities of daily living (ADLs); (ii) the opportunity to tailor treatment modalities to the individual; (iii) tasks can be subjectively entertaining [13], thereby circumventing issues associated with demotivation. The aim of this article is to provide a systematic review of the evidence available on effectiveness of VR technology in improving cognitive performance in patients with TBI, and translation into real-life situations.

Methods

The framework for this literature review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14] The protocol for this systematic review is registered on PROSPERO (CRD42017064705).

Search Strategy

Relevant articles (n=324) were identified by authors SM and MZ by performing a systematic search across multiple databases (Web of Science, PubMed and Embase) for full text articles in English from January 1947 to June 2017 (**Figure 1**). Difference in opinion on study inclusion was settled by consensus between authors.

The bibliographies of relevant articles and review articles were screened for additional citations of relevance.

Study Inclusion

All articles demonstrating the use of VR for cognitive rehabilitation in patients of any age who had previously sustained TBI of any severity were included (n=13). Articles demonstrating use in acquired brain injury were evaluated for any participants with traumatic aetiology before inclusion. If the results did not differentiate between TBI participants and other acquired brain injury participants, the study was excluded. Review articles, commentaries, and studies using VR for assessment of cognitive performance or diagnosis of cognitive deficit alone were excluded.

Data Analysis

All included studies (n=13) were evaluated according to study design, patient cohort, VR intervention[15] (**Figure 2**), method of assessment, and outcomes. Methods of assessment were defined descriptively and special attention given to inclusion of tests of translation into real-life performance. SIGN checklists were used for assessment of the internal validity and overall quality of RCT and comparative studies. The ROBINS-I tool [16] was developed for use with non-randomised comparative studies by evaluating several different domains to identify the risk of bias. We adapted this tool for assessing case studies. Quality assessment was conducted using the Oxford Centre for Evidence-based Medicine Levels of Evidence 2011 (see **Table 1**). Critical appraisal of all included articles was performed by authors LW, MP, and MA. Heterogeneity of included studies resulted in descriptive analyses being performed without meta-analysis.

Results

Study characteristics

Of all included studies (n=13), there was a combination of RCT (n=4), comparative studies (n=3), and non-comparative studies (n=6) (**Table 2)**. One comparative study was a cross-over study [17]. Two non-comparative studies evaluated all acquired brain injury patients, meaning that patients that had previously suffered a stroke were also included: one study had one patient with TBI and three stroke patients [18], and another study had four patients with TBI and eight stroke patients [19].

Patient Cohort

From all included studies (n=13), a total of 132 patients were subjected to VR interventions. In studies reporting age (n=11), the mean age of participants was 36.1 years (range: 20,67; SD=14.7), and of those that distinguished between gender (n=10), 74.5% of participants were male and 25.5% were female. Of studies reporting TBI severity (n=6), a total of 59 participants sustained severe TBI and four participants sustained moderate TBI. In the remaining studies (n=7), one study had 20 participants who were classified as having sustained mild-to-moderate TBI but were not distinguished [20], another study had 14 participants who were classified as having sustained moderate-to-severe TBI but were not distinguished [21], and the other studies (n=5) did not report severity of TBI. Of studies reporting time elapsed since traumatic injury (n=9), the mean time was 130.5 weeks (range: 2,224; SD=286.2), or 32.6 months. One study of 37 participants reported a minimum of three months since traumatic injury [22], and remaining studies (n=3) did not report the time elapsed.

Cognitive parameters

Included studies assessed a wide range of cognitive parameters. Most studies (n=10) focused on a single parameter and some studies (n=3) assessed multiple parameters. Cognitive outcome measures (**Table 3**) included learning and memory (n=4), attention (n=4), executive function (n=3), psychological attitude towards driving/ risk of road rage (n=1), route learning (n=2), community skill performance (n=1), and problem solving with clerical tasks (n=1).

VR interventions

With respect to methodology, VR interventions were either task-oriented (n=5), game-based (n=2), or IADL-based (n=6). With respect to immersion, VR interventions were either fully- (n=6), semi- (n=3), or non-immersive (n=4). Some studies involved advanced technology such as robotic arms with haptic cues (n=2) or artificial intelligence (AI) assisted systems (n=1), and others involved vehicle simulators (n=2), navigation tasks (n=2), or simulations of real life environments (n=3). With respect to temporal aspect of interventions, the mean time period over which interventions were carried out was 11.1 days (range: 1,42; SD=13.4) (n=8), the mean number of sessions was 10.7 (range: 1,15; SD=3.2) (n=11), and the mean duration of each session was 18.1 minutes (range: 4,90; SD=18.2) (n=9). Overall time period and number of sessions were not reported in some studies (n=5, n=2). Duration of each session was not reported in some studies (n=4), one of which reported number of trials but not the duration of each trial [23].

Outcomes

Neuropsychological assessment tools (n=8) (**Table 5**), performance on the VR interventions (n=4), and translation of improvements into real-life outcome (n=4) were used as tools to measure outcome. Real-life outcome measures included post-intervention employment rate [20], performance in real-life supermarket tasks [24], and performance of normal community based tasks [18]. One study used functional magnetic resonance imaging (fMRI) to assess changes in brain activity during a paired word association memory task pre- and post-intervention [25], and another study only used a simple questionnaire on attitude towards driving to assess the risk of dangerous driving [26].

Statistically significant improvement in cognitive parameter(s) was reported in ten studies. These mostly involved a range of neuropsychological assessment tools but one study demonstrated post intervention increases in blood oxygen level-dependent (BOLD) signal in several brain regions using functional magnetic resonance imaging (fMRI) [25], and two studies demonstrated translation of improvement into corresponding real-life tasks [18,22]. One study demonstrated a significant improvement in learning and attention but not in memory function [17], and another study demonstrated improvement in neuropsychological measures but this did not translate into an improvement measures of 'real-life' employment [20].

No significant differences were found in terms of topographical behaviour and spatial representations in TBI patients when the effectiveness of virtual and real environments were compared for rehabilitation. For example, no differences were found for route learning tasks, but superior performance on a spatial awareness assessment task in the real environment group was observed [21]. With respect to performance within VR environments and translation into real life, a study using a VR model of a shopping mall ("VMall") did not report a significant improvement post-intervention[24]. One study compared two different learning paradigms using virtual environments but did not evaluate the use of virtual environments alone to assess its specific contribution to an improvement in cognitive parameters [23]. With respect to level of evidence, two studies were level 1, three studies were level 2, two studies were level 3, and six studies were level 4 evidence (**Table 4**).

Discussion

The results of this systematic review demonstrate that there is a considerable body of evidence supporting the potential for the use of VR in the cognitive rehabilitation of patients with TBI. The total patient cohort across all included studies showed a significant male preponderance and mean age of 36.1 years. This is consistent with the demographics of patients with TBI: commonly young male individuals[2]. The mean time elapsed since TBI was 32.6 months, which demonstrates that the timing of appropriate allocation of VR interventions would not necessarily negate their efficacy. The wide range of 10 weeks to >15 years since trauma demonstrates a wide window for potential use of the intervention, and suggests that VR can be used for both patients with TBI in the community at present and prospectively as part of a rehabilitation programme for patients sustaining TBI. Further studies are required to explore the possibility of an interval-dependent effect on the extent of improvement as a result of VR intervention, or to identify the optimal time at which maximal benefit can be derived from VR interventions.

Randomised controlled trials

Our search yielded four RCT studies [20,22,24,26], which all showed a potential use for VR in cognitive rehabilitation. Common limitations include an unblinded approach, small sample sizes, unreported confounding factors such as IQ and neuropsychiatric deficits, and a lack of performance validity indicators, which is important to assess in TBI samples[27,28]. Cox et al. [26] studied changes in driving attitude in post-TBI military personnel when subjected to VR driving simulator sessions. Participants had suffered at least one closed head injury during previous deployment. Whilst the results demonstrate an improvement in driving attitude measured by a questionnaire, there are several limitations: (i) the control group did not receive a comparable placebo VR activity, meaning that the effects could potentially be the result of the increased interaction and engagement received by the treated group, (ii) there was no evidence of real world translation, (iii) a small sample size (six patients in the VR group and five patients in the control group) with a sub-optimal statistical approach using multiple t-tests rather than ANOVA limits the applicability of results, and (iv) PTSD rate was not reported in the sample, which may account for cognitive sequelae, especially in mild TBI[29]. Jacoby et al. [24] studied the use of a VR supermarket model for improving executive function in patients with TBI, compared with occupational therapy controls. The large effect sizes seen, although non-significant, is supportive of a beneficial role of VR. However, whilst there were no significant statistical differences between the participants allocated to the experimental and control groups, there was a trend towards the experimental group having less severe TBI, a younger age, and more education. Also, the randomisation schedule was changed during the study, and it is unclear if this resulted in researchers being unblinded to treatment allocation. The authors acknowledge that differential enjoyment of tasks may have resulted in group differences in motivation, which could also partly explain the reported effects. Thus, whilst the findings of this study are encouraging, more robust data is required to further validate its conclusions.

One study [20] employed an artificial intelligence (AI) assisted 3D VR system with clerical task oriented content to evaluate its effect on problem solving skills and employment outcomes. The VR group showed better performance on neuropsychological assessment post-intervention compared to control, but this did not translate into differences in employment outcomes. This highlights the difficulty of translating enhanced performance on rigidly assessed outcome measures to real-world activities, and the importance of assessing real-world translation whenever possible to reliably conclude on the benefits of treatment. Whilst this study had a larger sample size of 40 participants, 20% of participants dropped out per arm, and several basic demographics were unreported. Also, for the measures on which differences between VR group and control group were found using the Wisconsin Card Sorting Test (WCST), there was a trend towards the VR group performing better than the control group in pre-training. This may partly explain the superiority of the VR group performance post-intervention, however these pre-training differences were not statistically significant. The fact that participants were reported to enjoy the VR approach supports the advantage of VR in maintaining motivation during potential treatment. Despite its limitations, the basic experimental design and thought process behind the VR intervention is an encouraging marker of the directions that VR therapy could potentially take.

Another study [22] assessed the effect of a PC based VR program for ADL on prospective memory of patients with acquired brain injury, which also included TBI. Prospective memory (PM) is the capacity to remember to perform an activity at a dedicated time in the future: an ability that is often compromised in TBI survivors. Compared to participants receiving control treatment, participants assigned to a VR training program designed to improve PM in a virtual convenience store showed improvements on several outcome measures, although these failed to reach statistical significance. The reliability of outcome measures is unclear since the use of VR outcomes in this study appear to be a novel assessment tool. Also, the pre- versus post-test differences in VR measures in the experimental group could potentially reflect a practice effect. Since the control group did not seem to receive any tasks designed to tax PM specifically, in contrast to the VR treatment group, it is unclear whether their improved performance is due to the use of VR *per se* or due to the emphasis on improving PM in the treatment group. Evaluation of motivation would have been beneficial since the two groups have had a differential level of engagement in the study at post-test. Nonetheless, improvements in VR test measures in the treatment group were seen to transfer to real-life test measures. Further studies with more reliable assessment tools and equally engaging control interventions in patients with TBI alone are required.

Comparative studies

Our literature search yielded three comparative studies. Grealy et al. [17] studied the use of a VR bike-riding simulator on patients with severe TBI for improving cognitive functions. Results showed significant improvements in attention and learning but not memory functions. However, control subject data was drawn from a database of previous cases and numerous potential confounding factors were undisclosed such as TBI severity in the controls compared to the VR group. The fact that the authors only demonstrate improvements in cognition by comparing performance of the experimental group both before and after the intervention, with the performance of 'control' subjects who completed the cognitive assessments only once significantly undermines the results of the study. There may, therefore, be a large practice effect in the cognitive measures, but the experimental design cannot separate this from any treatment effect. Comparison of VR group post-intervention cognitive performance with 're-test' cognitive data obtained from controls would be required to achieve this. Also, it is unclear whether the benefits in performance observed are due to VR itself or purely due to exercise. There are well-documented effects of cardiovascular exercise upon cognition, thought to occur via upregulation of plasticity related proteins such as BDNF [30,31]. In order to determine whether VR accounts for any of this effect, a group of TBI survivors subjected to a non-VR exercise intervention is required. This study suggests a VR approach could be useful in TBI rehabilitation but the design does not offer a robust test of that proposition and no transfer effect is reported.

Lloyd et al. [23] studied the use of VR for route learning in patients with TBI. It is difficult to draw any reliable conclusions from this study as it presents a novel assessment tool. Also, the measures are obtained based on the experimenter controlling the VR software, which leaves the potential for experimenter bias in driving behaviour across the two conditions. This study does not reliably demonstrate the effectiveness of VR-based rehab in TBI *per se* as there is no control group in the strict sense of the term. However, it does show, via a within-subjects design, that when using a VR based approach to spatial navigation assessment and rehabilitation in brain injured patients, errorless training approaches may be preferable. Another study [21], compared VR and real environments (RE) for route learning and found the same pattern of route learning in both environments. Environment did not differentially impact TBI survivors' performance in completing a spatial navigation task, suggesting that VR may provide a potential alternative to RE rehabilitation. Their results show that recall of routes is comparable between VR and RE, which suggests that VR interventions do not provide a benefit to TBI survivors over real world training, at least in the context of spatial navigation. Furthermore, on several measures, there was a trend towards participants in the VR group performing worse suggesting that learning was affected. However, it cannot be guaranteed that VR and RE routes were of equal difficulty, which may explain the trend towards poorer performance in the VR group. Indeed, the VR was a replica of the RE that the control group experienced- but no direction names or street names were included in the VR district meaning that subjects had fewer cues in this condition, which may have affected their performance or made it more difficult than real-world navigation. Furthermore, no details were given of the RE group and their motor skills compared to the VR group. In summary, current evidence for the use of VR interventions for improvement of route learning and spatial representations in TBI survivors is insufficient.

Non-comparative studies

The majority of studies yielded by our search were non-comparative. Whilst they collectively indicate the potential benefit of VR interventions for cognitive rehabilitation, they are insufficient to draw any firm conclusions due to their experimental design and lack of controls. One study [32], demonstrated visuo-spatial improvement on neuropsychological assessment in a patient with severe TBI after a PC videogame driving simulator based intervention. Interestingly, there was increased activation of hippocampal and parahippocampal regions on fMRI post-VR, raising the possibility of enhanced memory function. Another study [33] used a novel VR system with a robotic arm providing haptic cues in a target acquisition task, which was received well by users and a reduction in frequency of problematic behaviour was noticed during treatment. The same group [13] corroborated these findings and demonstrated potential benefits to attention in patients with severe TBI. Yip & Man [18] demonstrated the use of VR based community skills training in a group of patients with acquired brain injury, of which one had sustained TBI. Both improvement in skills acquisition and memory performance, and translation into real-life task performance was observed. In summary, although non-comparative studies cannot fully validate the use of VR, several ideas such as the use of fMRI to correlate findings with the activation of particular regions of the brain, and the use of more advanced VR based interventions that are likely to be more engaging and subsequently maintain patient motivation, suggests that there are many promising future directions for the use of VR in cognitive rehabilitation.

Limitations

The use of VR for cognitive rehabilitation in TBI is a novel topic that is rapidly advancing in conjunction with technology. Therefore, there is limited evidence of its use in the literature, and there was insufficient data to perform any meta-analyses. Subsequently, case studies were also included to illustrate a more detailed account of current advances. VR interventions are diverse, ranging from simple game console based tasks [23] to the use of robotics [13,33]. Thus, rapid advances over the years means that the use of technology across included studies is not truly uniform. One example of future directions for VR-based rehabilitation strategies is the Oculus Rift DK2 (Oculus, Menlo Park, CA, USA) system, a VR headset which provides higher degrees of immersion. Studies of its efficacy in VR-based approaches to neuropsychological assessment[34] and balance [35] in non-pathological cohorts suggest that it may be an effective tool for use in TBI cohorts in future.

Conclusions

In conclusion, the use of VR for cognitive rehabilitation in patients with TBI appears to be a promising tool that could form a key component of the larger rehabilitation process. It allows the possibility for individualised treatment plans both in terms of content and pace. Since it may be more engaging than conventional rehabilitation, it is likely to be a more enjoyable experience for the patient and subsequently optimise improvement. However, several factors must be addressed in future studies: (i) differentiation between TBI severity to accurately assess VR efficacy, (ii) standardised neuropsychological assessment tools for specific cognitive parameters, (iii) development and testing of VR tools for assessment of cognition, (iv) use of performance validity should be addressed, (v) well-matched controls with equivalent non-VR interventions, (vi) assessing translation into real-life outcomes, and (vii) long term follow up to ensure positive effects are not transient.

Figure 1- Flowchart depicting multi-database literature search for of VR for cognitive rehabilitation in TBI patients

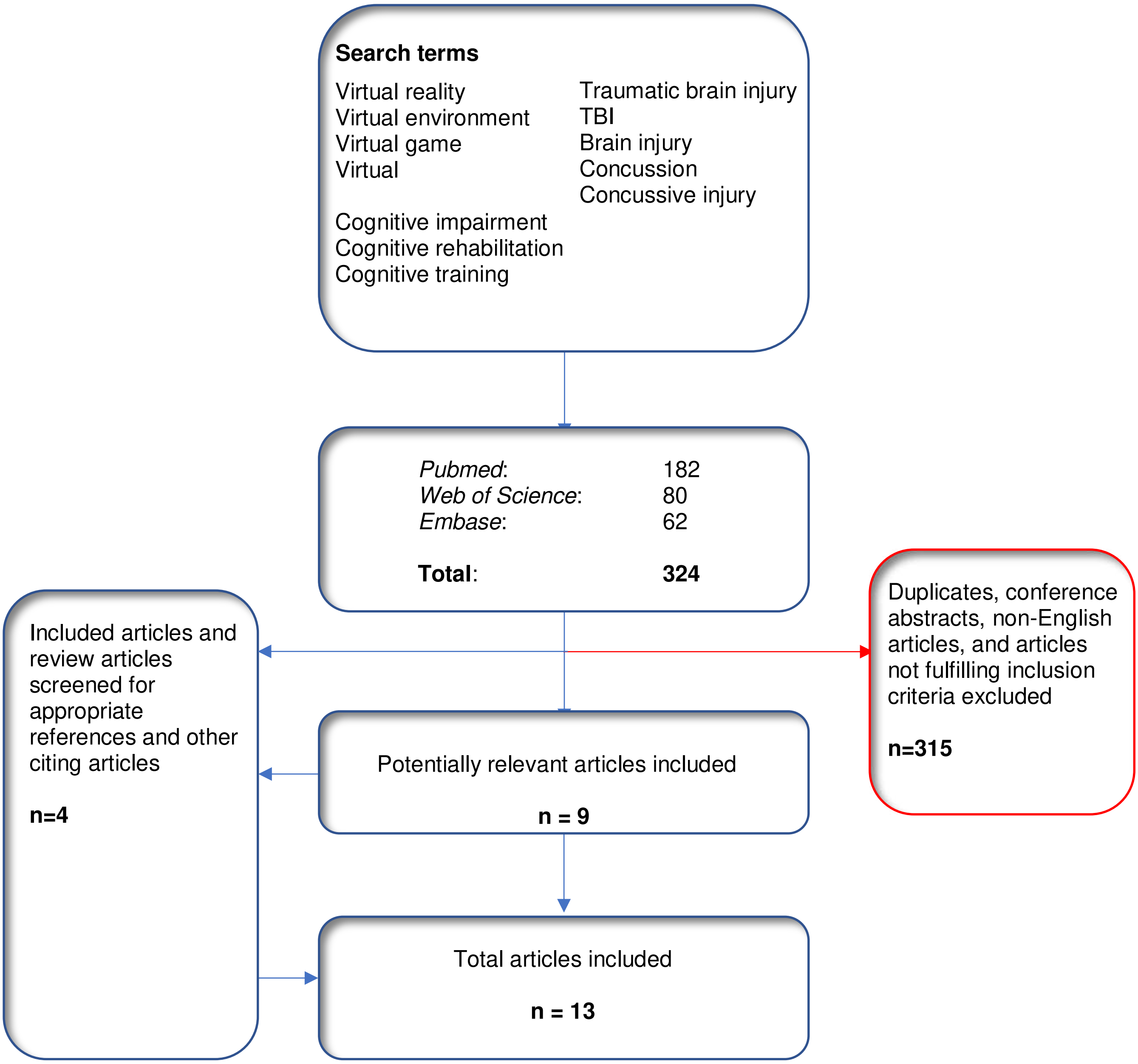

Figure 2- This flow-chart summarizes methodology used for evaluation of VR interventions in retrieved studies.

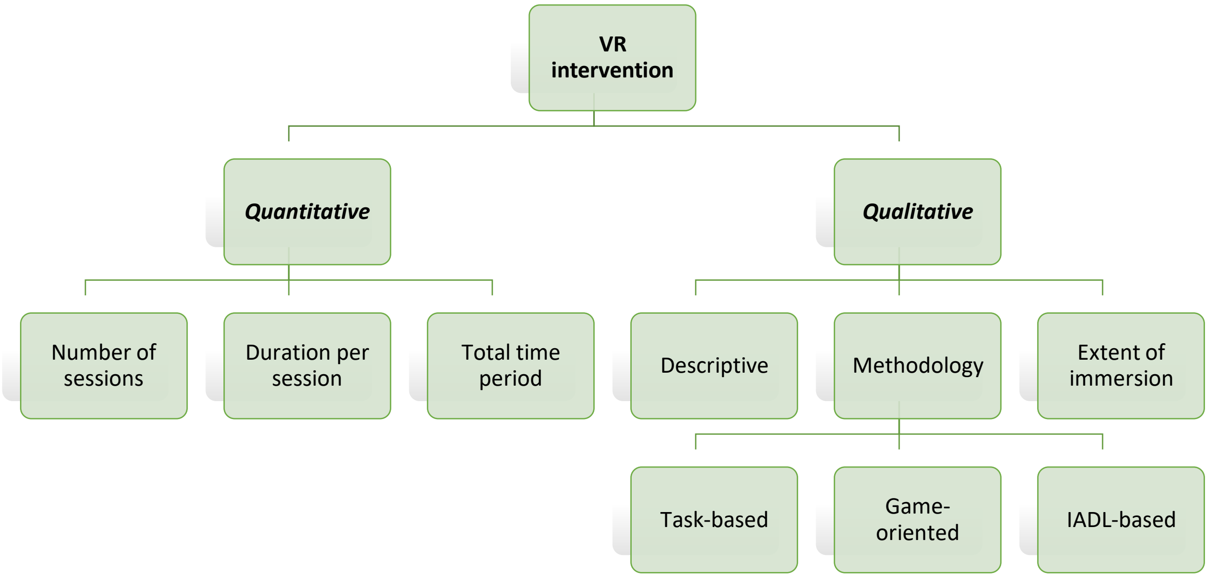

Table 1- levels of evidence (adapted from Oxford Centre for Evidence-based Medicine 2011)

Level of Evidence	Description
1	Systematic reviews (with 'homogeneous' RCTs), individual high quality RCT (with 'narrow' confidence intervals)
2	Systematic reviews (with 'homogeneous' cohort studies), individual low quality RCT, individual cohort studies
3	Systematic reviews (with case-control studies), individual case control studies
4	Case series, case reports, low quality case control studies

Table 2- summarises studies included from literature search

Study	Participants	TBI severity	Cognitive parameters	Virtual reality intervention							Outcomes measured
				Details	*Methodology*			*Immersion*			
					Task	Game	IADL	Full	Semi	Non	
Grealy et al 1999	13 patients who sustained severe TBI 1.7-178 weeks prior, compared with >25 matched controls	Severe	Learning and memory Attention	VR bike riding simulator 12 sessions, 25 mins each, 3 per week, 4 weeks		X		X			Significantly better than controls post-intervention tests of attention and learning Memory functions did not improve
Lloyd et al 2009	8 patients with TBI sustained 206±105 mths prior, errorful vs errorless learning paradigm in VE	Unreported- inclusion criterion of evidence of memory deficits	Route learning	VE navigation task, control pad operated by experimenter in response to user command Demonstration trial, 2 learning trials, test trial	X					X	Significantly greater number of errors during route recall in errorful learning paradigm compared to errorless learning paradigm
Yip & Man 2009	Adult male, 30 months since injury (and three other patients post stroke)	Unreported- inclusion criterion one or more cognitive deficits affecting community integration	Task specific Transfer to real environment Skills acquisition Functional independence Global cognitive ability	VR based community skills training 10 sessions, 35-40 mins each, 3 per week			X			X	Skills acquisition and memory performance improved Improvement in real-life task performance
Cox et al 2010	Post-TBI military personnel- 6 patients in VR group compared with 5 in control	Unreported- participants already participating in rehabilitation programme for TBI	Questionnaires on road rage and risky driving behaviour	Ford T driving simulator 4-6 sessions, 60-90 mins each			X	X			Significant reduction in road rage and risky driving in VR group only
Gamito et al 2011	20y male with severe TBI sustained 3 months prior	Severe	Memory Attention	Online 3D platform with VR simulation of ADL			X	X			Significant increase in correct responses between initial and final PASAT assessment

				10 sessions							
Larson et al 2011	18 participants aged 19-73y with severe TBI sustained 2-71 weeks prior	Severe	Attention Subjective responses to VR	VRROOM system with robotic arm providing haptic cues 6 trial blocks per day, 4 mins each, 2 days	X			X			15/18 users completed all blocks Frequency of problem behaviour declined during treatment Target acquisition time decreased over consecutive blocks Haptic cue (nudge) significantly aided target acquisition
Caglio et al 2012	24y male, with moderate TBI sustained 1y prior, and 5 months rehab unsuccessful	Moderate	Learning and memory Frontal executive function	PC videogame driving simulator 90 mins per session, 3 per week, 5 weeks		X				X	Visuo-spatial improvement shown with neuropsychological assessment post-VR Increased activation of several brain regions on fMRI post-VR
Sorita et al 2012	27 participants with moderate-severe TBI, route learning in VE vs RE	Moderate-severe	Route learning Spatial representation	VE on large video projector controlled with joystick	X				X		Same pattern of route learning in both VE and RE Spatial representation similar between groups (RE group significantly better on scene arrangement test)
Dvorkin et al 2013	21 participants sustained severe TBI 10.3±15.6 weeks prior	Severe	Attention Subjective responses to VR	VRROOM system with robotic arm providing haptic cues 6 trial blocks per day, 4 mins each, 2 days	X			X			Well tolerated by 18/21 users, with improvements in behaviour Significant reduction in attention loss during a task Haptic nudge beneficial for learning Progressive improvement in target acquisition

Jacoby et al 2013	12 participants aged 19-55y sustained moderate-severe TBI, several with DAI, VR vs occupational therapy controls, 6 per group	Moderate-severe	Executive function ADL performance and transfer to real life	VMall 10 sessions, 3-4 per week			X		X		No significant differences but larger effect sizes in VR group suggest potential advantage
Man et al 2013	40 participants aged 18-55y with mild-moderate TBI, VR vs psycho-education control, 20 per group	Mild-moderate	Problem solving Employment outcome at follow-up	AI assisted 3D VR system with clerical task oriented content 12 sessions, 20-25 mins each			X	X			VR group showed better performance on neuropsychological assessment post-intervention than control No difference in employment outcomes
Yip & Man 2013	37 participants with brain injury acquired at least 3 months prior, VR compared with reading/ games control	Unreported	Prospective memory Real life outcome	PC based VR program for ADL 12 sessions			X			X	Significant changes in both VR based and real-life based outcome measures
Simmons et al 2014	4 participants with TBI (further 8 post stroke)	Unreported	Executive function (and motor function) Independent living skill	3D PreMotor exercise games	X				X		Significant improvement shown by EFPT assessment

Table 3- table summarising cognitive parameters tested in included studies

Cognitive parameters	Studies
Learning and memory	Grealy et al 1999, Yip & Man 2013, Caglio et al 2012, Gamito et al 2011
Attention	Grealy et al 1999, Gamito et al 2011, Larson et al 2011, Dvorkin et al 2013
Executive function	Simmons et al 2014, Jacoby et al 2013, Caglio et al 2012
Community skills	Yip & Man 2009
Problem solving	Man et al 2013
Route learning	Lloyd et al 2009, Sorita et al 2012
Driving attitude	Cox et al 2010

Table 4- summarises study types and level of evidence of included studies from literature search

Study	Type	Level of Evidence
Jacoby et al 2013	RCT	1
Man et al 2013	RCT	1
Cox et al 2010	RCT	2
Grealy et al 1999	Comparative	2
Yip & Man 2013	RCT	2
Lloyd et al 2009	Comparative	3
Sorita et al 2012	Comparative	3
Yip & Man 2009	Non-comparative	4
Gamito et al 2011	Case study	4
Larson et al 2011	Non-comparative	4
Caglio et al 2012	Case study	4
Dvorkin et al 2013	Non-comparative	4
Simmons et al 2014	Non-comparative	4

Table 5- summarises neuropsychological tests used to assess cognitive function parameters across included studies

Reference	Cognitive function parameter	Test	Statistical Effect	Time points
Grealy et al 1999	Learning	Auditory verbal learning (Rey) Visual learning (AMIPB)	$F_{1,8}$=7.48, p<0.05	Compared changes between pre- and immediate post-intervention performance against control population mean (note: digit span excluded as scores from control population were skewed)
	Memory	Logical memory learning (AMIPB) Complex figure tests (Rey)	$F_{1,11}$=0.14, p=0.71	
	Attention	Digit span (forward and backward) Digit symbol (WAIS-R) Trails A and B tests	$F_{2,18}$=5.93, p<0.05	
Lloyd et al 2009	Route learning	Errorless and errorful learning condition paradigms	t(20) = 2.631, p=0.016, partial eta^2=0.267	Errors during route recall on two different paradigms assessed in same participants- errorless learning more effective
Yip & Man 2009	Community living skills	Training software parameters Behavioural checklist for RE Self-efficacy questionnaire NSCE-CV Lawton IADL-CV	No statistical tests, but improvement in all 4 cases across all parameters	Pre- and immediate post-intervention tests
Cox et al 2010	Driving attitude	Road Rage Questionnaire	Pre: 27.2 ± 6.4, post: 23.6 ± 9.9 p = 0.01	Pre- and immediate post-intervention measures, performance on simulator also improved significantly across several measured variables
		CARDS	Pre: 27.2 ± 15.3, post: 11.2 ± 7 p < 0.05	
Gamito et al 2011	Memory Attention	PASAT assessment	Trial 1: Pre vs int: $\chi2(1, 59) = 23.438$; p < 0.001) Int vs post: ($\chi2(1, 59) = 41.667$; p < 0.001) Trial 2: Pre vs int: ($\chi2(1, 59) = 4.356$; *p* < 0.05) Int vs post: ($\chi2(1, 59) = 5.689$;	Pre-intervention (pre), intermediate (int), and immediate post-intervention (post) assessments

			p < 0.05)	
Larson et al 2011	Attention	VR-adaptation of APT	F(2,28)=3.925, MSE=14.116, p<0.031	Target acquisition time recorded for first 23 trials of each block of 12
Caglio et al 2012	Learning and memory	Corsi block-tapping test Corsi's supraspan test Auditory verbal learning (Rey) RBMT	RAVLT immediate recall (z adjusted = 1.99, p=0.05) Corsi's supraspan test, delayed recall (z adjusted = 1.96, p = 0.05) Corsi's supraspan test, immediate recall (z adjusted = 2.12, p = 0.05) Remaining were either non significant or insufficient data	Pre-intervention, and immediate, 2 months, and 1 year post-intervention
	Attentional-executive functioning	Trail making test ADAS		
Sorita et al 2012	Route learning	Error rate during route recall	No significant effect of environment on learning	Immediate and delayed route recall after route learning task in RE and VE
Dvorkin et al 2013	Attention	VR-based target acquisition task	Between visits: (F(1,17) = 20.2, p = 0.0003) Between blocks: (F(5,85) = 8.95, p < 0.0001)	12 blocks of trials over the course of 2 days, with target acquisition times measured at all points
Jacoby et al 2013	Executive function	Executive function performance test	VR: 35.5% improvement in scores but not significant VR vs non-VR improvement: Z=-1.761, p=0.046, ES=0.51	Pre- and immediate post-intervention assessments
	RE transfer	Multiple Errands Test- simplified version	VR: 46.2% improvement in scores but not significant VR vs non-VR improvement: Z=-1.761, p=0.046, ES=0.51	
Man et al 2013	Problem solving	Wisconsin Card Sorting Test Tower of London test Vocational Cognitive Rating Scale	WCST-% errors (p=0.02) WCST-% conceptual level response (p<0.01) Remaining non significant	Pre and immediate post-intervention assessment and compared effect size between VR and control
Yip & Man 2013	Prospective memory	VR based memory test Behavioural checklist for RE CAMPROMT-CV Hong Kong List Learning Test Frontal Assessment Battery	Significant differences in real life behavioural checklist, HKLLT, FAB, WFT-CV and CTT	Pre- and 1 week includepost-intervention assessments, and comparisons between VR and control groups

		World Fluency Test- Chinese version Colours Trail Test CIQ-CV Self efficacy questionnaire		
Simmons et al 2014	Executive function	Executive function performance test	Significant improvement in 3 of 4 components of EFPT-skill scores and in 1 of 4 components of EFPT-task scores	Pre- and immediate post-intervention measurements

Abbreviations: ADAS- Alzheimer's disease assessment scale; AMIPB- Adult Memory and information Processing Battery; APT-attention process training; CAMPROMT-CV- Cambridge Prospective Memory Test- Chinese Version; CARDS- Cox Assessment of Risky Driving Scale; CIQ-CV- Chinese Version of the Community Integration Questionnaire; CTT- Colour Trails Test; FAB- frontal assessment battery; HKLLT- Hong Kong List Learning Test; Lawton IADL-CV- Lawton Instrumental Activities of Daily Living Scale-Chinese Version; NCSE-CV- Neurobehavioural Cognitive Status Examination-Chinese Version; PASAT- Paced Auditory Serial Addition Task; RBMT- Rivermead Behavioural Memory Test; WAIS-R- revised Wechsler Adult Intelligence Scale; WCST-Wisconsin Card Sorting Test; WFT-CV- Word Fluency Test- Chinese Version; RE- real environment.

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